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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/944,360	09/04/2001	Teruaki Sekine	2001_1248A	1329

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EXAMINER

DAVIS, MINH TAM B

ART UNIT PAPER NUMBER

1642

DATE MAILED: 03/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/944,360

Applicant(s)

SEKINE ET AL.

Examiner

MINH-TAM DAVIS

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 December 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 24-35 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 24-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date <u>08/09/04</u> |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/1/08/04 has been entered.

Accordingly, claims 24-35 are being examined.

The following are the remaining rejections.

OBJECTION

Claims 30-35 are objected to because they are drawn to the same method as claims 24-29, respectively.

Applicant is advised that should claims 24-29 be found allowable, claims 30-35 will be rejected under 35 U.S.C. 101 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to reject the other as being a substantial duplicate of the allowed claim. See MPEP 706.03(k).

REJECTION UNDER 35 USC 103, NEW REJECTION

Claims 24-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sekine T, 1994, Human cell: Official J human cell res society (Japan): 7(3): 121-4, of record, in view of Sasaki Y et al, J Hepato-biliary-pancreatic surgery, 1998, 5(1): 14-17.

Claims 24-35 are drawn to:

A method for preventing recurrence of liver cancer for five years, comprising administering activated lymphocytes while performing treatment of cancer, which is surgical operation (claims 24, 30). The lymphocytes are collected from a cancer patient or the other cancer patient (claims 25, 31), and cultivated for proliferation or activating, said lymphocytes having cells of more than 1×10^9 per millimeter (claims 26, 32). The activation is in the presence of solid phase anti-CD3 antigen and interleukin 2 (claims 27, 33). The activated lymphocytes are administered within eight months after commencing said treatment of cancer, wherein said lymphocytes could be administered at least five or more times (claims 28-29, 34-35).

Sekine et al teach prevention of recurrence of hepatocellular carcinoma after culative operation, by infusion of autologous lymphocytes that have been activated and expanded by cultivation with immobilized anti-CD-3 antibody and IL-2 (abstract). Sekine et al teach that recurring-free survival rates are up to 24 months from 49 treated patients, with a recurrence in 13 cases of 49 treated pateints (p.5-6 and figure 3 on p.7).

Sekine et al do not teach that prevention of recurrence of liver cancer for five years. Sekine et al do not teach administering activated lymphocytes while performing surgical treatment of liver cancer. Sekine et al do not teach that the lymphocytes are

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collected from other cancer patient, and that said lymphocytes have cells of more than 1×10^9 per millimeter.

Sasaki et al teach that the five year survival rate for liver cancer patients, in stage II, who underwent hepatic resection (HR), and had good liver function is 64%, and even for those patients in stage II with bad liver function (clinical stage II), the five year survival rate is 32% (abstract and figure 1 on page 15).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to use the method of Sekine et al for preventing recurrence of liver cancer after surgery. It would have been obvious to administer activated lymphocytes while performing surgery treatment of cancer, because one would have expected that the same result would be obtained, wherein treatment with activated lymphocytes is complementary to surgery. Although Sekine et al do not teach that the prevention of recurrence of liver cancer for five years, one would have expected that the same results would be obtained with the method of Sekine et al, because the method taught by Sekine et al seems to be the same as the claimed method, and because with hepatectomy alone, the five year survival rate for patients, in stage II, who underwent hepatic resection (HR), and had good liver function is 64%, and even for those patients in stage II with bad liver function (clinical stage II), the five year survival rate is 32%, as taught by Sasaki et al.

Further, it would have been obvious that the lymphocytes are collected from other cancer patient, to provide more lymphocytes. With regards to the amounts of

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lymphocytes recited in claims 26, 32, to determine optimum concentration of reactants is within the level of ordinary skill in the art. See *In re Kronig*, 190 USPQ 425.

ANSWERS TO APPLICANT'S ARGUMENTS

Applicant argues that the results of Sekine's two year study fail to suggest the prevention of recurrence of liver cancer for five years. Applicant argues that Sekine et al teach away from the prevention of 5 years, because Sekine et al disclose that the recurrence rate for liver cancer is 33% in the first year, 57% in the second year, and 70% in the third year, and that no preventive method is known. Applicant argues that thus there is no expectation of success based on the teaching of Sekine et al.

Applicant argues that thus the instant invention is surprising and unexpected because the Examiner's assertion in a telephonic interview that cancer patients are alleged to live at least five years following a surgical removal of the liver is inconsistent with the high recurrence rate disclosed by Sekine.

Applicant's arguments set forth in paper of 12/08/04 have been considered but are not deemed to be persuasive for the following reasons:

The results of claimed invention are not surprising and unexpected. Although Sekine et al do not teach that the prevention of recurrence of liver cancer for five years, one would have expected that the same results would be obtained with the method of Sekine et al, because the method taught by Sekine et al seems to be the same as the claimed method, and because with hepatectomy alone, the five year survival rate for liver cancer patients, in stage II, who underwent hepatic resection (HR), and had good

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liver function is 64%, and even for those patients in stage II with bad liver function (clinical stage II), the five year survival rate is 32%, as taught by Sasaki et al.

Concerning the disclosure of Sekine et al that the recurrence rate for liver cancer is 33% in the first year, 57% in the second year, and 70% in the third year, it is not clear whether these patients had hepatic resection, a limitation of the claimed method, and/or whether these patients had good or bad liver function, wherein those with good liver function, even in stage II, are expected to have a better survival rate after hepatic resection (HR).

Thus, Sekine et al do not teach away from the invention, and the teaching of Sasaki et al is not contradictory to the teaching of Sekine et al .

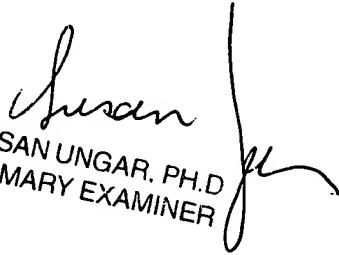
Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MINH TAM DAVIS

February 23, 2005


SUSAN UNGAR, PH.D.
PRIMARY EXAMINER